

CLAIMS

What is claimed is:

SubC 1 ✓
5

- 5 ~~1~~
- An inhibitor of a colony stimulating factor (CSF), which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising an agent which binds to a CSF, an agent which inhibits expression of a CSF, an antagonist of a colony stimulating factor receptor (CSFR), an antibody directed to a CSF or a CSFR, or an agent which inhibits activation of a CSFR, or a pharmaceutically acceptable salt thereof.
- 10 2. The inhibitor of Claim 1 wherein the CSF is a monocyte-colony stimulating factor (M-CSF).
3. The inhibitor of Claim 1 wherein the chemokine is a beta-chemokine.
4. The inhibitor of Claim 1 wherein the CSF is an M-CSF, the chemokine is monocyte chemotactic protein-1 (MCP-1), and the inhibitor is an antibody directed to an M-CSF or an antibody directed to a monocyte-colony stimulating factor receptor (M-CSFR).
- 15 5. The inhibitor of Claim 1 wherein the CSF is an M-CSF, the chemokine is MCP-1, and the inhibitor is an antagonist of an M-CSFR.
6. The inhibitor of Claim 1 wherein the CSF is a granulocyte-colony stimulating factor (G-CSF).
- 20 7. The inhibitor of Claim 1 wherein the chemokine is an alpha-chemokine.
8. The inhibitor of Claim 1 wherein the CSF is a G-CSF, the chemokine is IL-8, and the inhibitor is an antibody directed to a G-CSF or an antibody directed to a granulocyte-colony stimulating factor receptor (G-CSFR).

-38-

9. The inhibitor of Claim 1 wherein the CSF is a G-CSF, the chemokine is IL-8, and the inhibitor is an antagonist of a G-CSFR.
10. The inhibitor of Claim 1 wherein the CSF is a granulocyte macrophage-colony stimulating factor (GM-CSF).
- 5 11. A pharmaceutical composition, comprising an inhibitor of a CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, or excipient.
- 10 12. A method of treating inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising administering to a mammal, in need thereof, a therapeutically effective amount of an inhibitor of a CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, or a pharmaceutically acceptable salt thereof.
- 15 13. The method according to Claim 12 wherein the disease being treated is atherosclerosis.
14. The method according to Claim 12 wherein the disease being treated is sepsis.
- 20 15. The method according to Claim 12 wherein the disease being treated is asthma.
16. The method according to Claim 12 wherein the disease being treated is an autoimmune disease.
- 25 17. The method according to Claim 12 wherein the disease being treated is osteoporosis.

-39-

18. The method according to Claim 12 wherein the disease being treated is rheumatoid arthritis.
19. The method according to Claim 12 wherein the disease being treated is osteoarthritis.
- 5 20. A method for screening for an inhibitor of an M-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising analyzing an (M-CSF)-stimulated monocyte population using a Fluorescent Activated Cell Sorter technique.
- 10 21. The method according to Claim 20 wherein the (M-CSF)-stimulated monocyte population is analyzed in whole blood after red blood cell lysis.
22. The method according to Claim 20 wherein the screening method is a high throughput screening method.
- 15 23. The method according to Claim 20 wherein the (M-CSF)-stimulated monocyte population has also been stimulated by MCP-1.
24. The method according to Claim 23 wherein the (M-CSF)-stimulated monocyte population which has also been stimulated by MCP-1, is analyzed in whole blood after red blood cell lysis.
- 20 25. A method for screening for an inhibitor of a G-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising measuring binding of an (I^{125}) G-CSF to a G-CSFR in a (G-CSF)-stimulated neutrophil population.
- 25 26. The method according to Claim 25 wherein the screening method is a high throughput screening method.

27. A method for screening for an inhibitor of a GM-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising measuring binding of an (I^{125}) GM-CSF to a GM-CSFR in a (GM-CSF)-stimulated neutrophil population or analyzing a (GM-CSF)-stimulated monocyte population using a Fluorescent Activated Cell Sorter technique.
28. A method for screening for an inhibitor of a CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, the method comprising:
- Step (a) Obtaining CSFR cDNA and corresponding (I^{125})-CSF;
- Step (b) Cloning the CSFR cDNA of Step (a) into a vector;
- Step (c) Stably transfecting the vector of Step (b) into a hematopoietic cell line that resembles circulating leukocytes;
- Step (d) Quantitating the transfected vector of Step (c) and measuring the binding of said (I^{125})-CSF; and
- Step (e) Screening agents for inhibition of CSF activity using a binding assay comprising the transfected vector of Step (c) and said (I^{125})-CSF.
29. A method for screening for an inhibitor of an M-CSF which inhibits the synergistic effect of said CSF on chemokine-mediated inflammation, osteoporosis, an autoimmune disease, or atherosclerosis, comprising measuring binding of an (I^{125}) M-CSF to an M-CSFR in an (M-CSF)-stimulated monocyte population.
30. The method according to Claim 29 wherein the M-CSFR is a soluble M-CSFR.

add
a2
B2